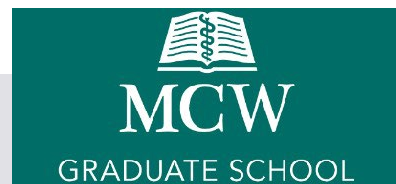


2024-25

# BIOCHEMISTRY

Degree Offered: Doctor of Philosophy



## Program Description

As a member of the Biochemistry PhD program at MCW you will have the opportunity to investigate the mechanistic basis of diseases including cancer, neurodegeneration, heart failure, diabetes and others, using state-of-the-art facilities and instrumentation for structural biology, metabolism, signal transduction, and drug discovery.

## Admission Requirements

In addition to the general [Graduate School admission requirements](#), this program has additional specific requirements.

Admission to the Biochemistry Graduate Program is through the [Interdisciplinary Program in Biomedical Sciences \(IDP\)](#), [Neuroscience Doctoral Program \(NDP\)](#), or [Medical Scientist Training Program \(MSTP\)](#). After completion of the first-year curriculum of that program, students who choose to complete their dissertation research project with faculty of the Biochemistry Graduate Program will have the opportunity to continue their graduate studies by selecting from among a wide range of courses that are offered within the Biochemistry Graduate Program as well as other programs at MCW. Courses to be taken are based on the student's interests in consultation with the student's dissertation advisor and committee.

## Fields of Study

The following areas of research are available in the department:

- The identification and characterization of signaling pathways that prevent cells from completing cytokinesis with unresolved mitotic errors.
- Structure/function studies of kinases and other proteins that ensure faithful progression through cytokinesis.
- Machine learning to predict and understand biology, enabling drug discovery and personalized medicine
- Mass spectrometry-based multi-omics (proteomics, metabolomics, lipidomics)
- Cancer cell signaling in neurological and other malignancies.
- Regulation of chromatin structure and accessibility by the conformation and dynamics of nucleosomal histone tails. Additional levels of regulation by histone post-translational modifications (PTMs) and histone variants.
- Post-translational modification of lysine and cysteine residues controls protein function and exploiting these insights in the design of novel chemical probes
- Functional study of the nutrient-dependent O-GlcNAc signaling in pregnancy, early development, and metabolism.
- Pre- and Post-natal exposure to non-nutritive sweeteners: impact on development and metabolism
- Heme protein interactions with the actin cytoskeleton, mitochondria and RNA regulating proteins, how these change with cellular environment and the downstream effects.
- Redox and calcium signaling in the heart and disruptions contributing to atrial fibrillation.
- Diabetes, beta cell biology, inflammation innate immunity, cell signaling, cell fate decisions.
- Molecular mechanisms underlying the functioning of mannose 6-phosphate receptors

(MPRs) in mammalian cells.

- Molecular regulation of nutrient utilization in metabolic syndrome, atherosclerosis and inherited diseases of fat metabolism.
- Molecular mechanisms governing G protein-coupled receptor signaling in mammalian cells.
- Structural biochemistry of multi-protein machinery (RNA polymerases and associated factors) involved in gene transcription and RNA processing in the eukaryote.
- Oxidative stress, reactive oxygen/nitrogen species, cell membrane lipids, lipid peroxidation and mechanisms of oxidative apoptosis.
- The role of metabolic modifications such as acetylation. The role of topological stress in DNA. The role of accessory proteins in modulating histone DNA interactions.
- Structure-function relationship of enzymes and receptors using X-ray diffraction methods.
- Characterization of molecular mechanisms of protein dynamics and protein-protein interactions using solution NMR and other biophysical techniques.
- In vivo mechanisms controlling developmental and cardiovascular specific gene expression.
- Druggability of proteins involved in mitochondrial homeostasis in healthy and diseased cells to identify molecular mechanism and novel therapeutic routes.
- Mechanistic differences of Ras/Raf-induced growth inhibition vs. proliferation at molecular levels.
- Protease and protease inhibitors in the cornea. Structure-function of maspin and its effects on carcinoma and corneal cells.
- Structural biology of immunological signaling molecules and the use of NMR spectroscopy in structural proteomics

## Credits Required to Graduate

60 credits minimum

## Required Courses

### **10222 Ethics and Integrity in Science.** *1 credit.*

This course provides the basis for understanding the ethical issues related to basic scientific and medical research, including animal and human subject research, fraud, and misconduct, and governmental, institutional, and researcher responsibilities. Bioethics 10222 is offered during the spring and summer terms only.

### **10444 Research Ethics Discussion Series.** *1 credit.*

*Prerequisite: 10222 Ethics and Integrity in Science.*

The course is directed by members of the Bioethics Faculty and provides facilitated discussions of a series of topics in research ethics. Discussions are led by members of the Basic Science faculty and are focused on ethical issues that commonly come up in biomedical research. The course is meant to not only reinforce the basic ethics taught in the online course Ethics and Integrity in Science, which is a prerequisite, but also to explore the gray areas of the individual topics. The intent is to offer students illustrative examples of ethical issues that might arise in their careers, to emphasize the ethical principles that apply in such situations, and to provide practical guidance on how these types of situations should be correctly handled. This course is offered as a discussion series. Students are expected to attend and participate in the discussion. Bioethics 10444 is offered during the spring terms only.

**02207 Enzyme Kinetics and Receptor Binding. 1 credit.**

This course teaches both the theoretical framework and practical aspects of enzyme kinetics and receptor binding studies. Topics covered include basic steady state kinetics including the determination and meaning of  $K_m$  and  $V_{max}$  values for simple and multisubstrate reactions, determination binding properties and kinetic consequences of common reversible inhibitors (competitive, non-competitive, uncompetitive, mixed), slow-on, slow-off inhibitors and irreversible inactivators. Dissociation constants and procedures for determining them will be discussed for both enzymes and macromolecular receptors. Practical methodologies for determining pre-steady state kinetics will be presented. Practical aspects of designing kinetic studies will be discussed and later sessions of the course will involve reading and student-led discussions of studies in the literature that illustrate ways in which studies of enzyme kinetics or receptor binding advanced the study of particular enzymes and other macromolecules. Over the six-week duration of the course each student will prepare a short report in which he or she describes the design and, if possible, execution of a series of kinetic or receptor binding studies that draw on the teachings of the course and are related to the work each proposes to carry out for a dissertation.

**02226 Biophysical Techniques in Biochemistry. 3 credits.**

*Prerequisite: 16268 Protein Chemistry: Principles*

This course will introduce the basic theory and practical applications of an array of biophysical techniques commonly used in biochemical research. Optical, fluorescence, and magnetic resonance spectroscopies, x-ray crystallography, mass spectrometry and kinetics techniques are just a sampling of the topics covered in this comprehensive course.

**02230 Biomolecular NMR: Structure and Molecular Recognition. 1 credit.**

*Prerequisite: 16268 Protein Chemistry: Principles*

Nuclear magnetic resonance spectroscopy (NMR) is a powerful tool for the interrogation of biomolecular structure and interactions at atomic resolution. Structural genomics efforts have produced refinements in the methodology for three-dimensional protein structure determination, such that new structures can be solved in a matter of weeks using increasingly automated processes. This course begins with a description of the quantum mechanical basis for multidimensional NMR using the product operator formalism. This powerful operator algebra rigorously predicts the propagation of the nuclear spin wavefunction under a time-independent Hamiltonian operator governing interactions between nuclear spins and between spins and static or transient magnetic fields, enabling the development of increasingly complex pulse sequences for multidimensional, multinuclear NMR measurements of biomolecules. Simple pulse sequences for magnetization transfer and isotope editing are described using product operators and combined into more complex two- and three-dimensional pulse schemes for triple-resonance correlation of nuclei in proteins. Systematic application of these NMR methods to the sequence-specific assignment of isotopically enriched proteins will then be linked to the interpretation of other types of NMR data (nuclear Overhauser effect; scalar and dipolar couplings) that report directly on tertiary structure. The balance of the course will consist of practical, hands-on training in basics of 2D/3D NMR data acquisition, processing, and analysis, as well as interactive computer tutorials on the chemical shift assignment and 3-D structure determination processes.

**02235 Biomolecular NMR: Protein Dynamics and Binding.** 1 credit.

*Prerequisites: 16268 Protein Chemistry: Principles and enrollment in 02230 Biomolecular NMR: Structure and Molecular Recognition.*

NMR spectroscopy is one of the most powerful tools of contemporary structural biology. Multiple NMR applications enable structural, thermodynamic, and kinetic analysis of proteins and nucleic acids under physiological conditions with site-specific resolution. The course "Biomolecular NMR: Protein Dynamics and Binding" discusses applications of NMR to protein dynamics, conformational transitions, and ligand binding. The topics include NMR line shape analysis and spin relaxation methods that are used to extract structural, thermodynamic, and kinetic parameters of conformational transitions and ligand binding in proteins. The course is directed to students who would like to utilize NMR spectroscopy as a part of the dissertation research.

**02240 Contemporary X-ray Crystallography.** 1 credit.

*Prerequisite: Completion of IDP course curriculum.*

X-ray crystallography is the main method that is used to elucidate three-dimensional structures of macromolecules and biomolecular complexes, and capable of revealing structural details at high resolutions. Powered by modern synchrotron-based light sources and state-of-the-art computer programs, contemporary crystallographic research has provided mechanistic insights into complex cellular functions such as gene transcription and translation. While crystallographic computer programs are openly available, the use of these packages by biologists who do not have a theoretical comprehension of crystallography can be unproductive. This course is designed to teach non-crystallographers the capability to intelligently use crystallographic programs that are available in the form of bundled software. Attendees will learn systematically the central theory behind the crystallographic tools in use today, and hence grow an appreciation of the physical process that takes place during an experiment to determine the structure of a protein or nucleic acid. A central aim of this is to generate stimulating discussions that will help the students grasp the essence of macromolecular crystallography.

**02248 Structural Basis - Macromolecules.** 1 credit.

With the explosion of the number of three-dimensional structures of biological macromolecules that have been determined, it is imperative to learn how to study their structures in detail and learn the molecular basis for their functions. This course discusses the mechanism of action and the relationship between structure and function of selected groups of biological macromolecules. The molecules studied range from enzymes (both soluble and membrane-bound) to proteins involved in signal transduction and in epigenetic gene regulation. At the end of the course, the student will attain the skills to analyze the relationship between structures and functions of proteins.

**02276 Special Topics in Biochemistry.** 1 credit.

Students are expected to develop an advanced understanding of various aspects of special topics in biochemistry through introductory lectures, outside readings, and in-class discussions.

**02295 Reading and Research.** 1-9 credits.

The course of study for Reading and Research is designed by each student with his/her advisor to focus on readings in literature in the student's field, to build bibliographic resources for the dissertation, and to conduct supervised, independent research.

**02301 Seminar. 1 credit.**

Students are given practice in presenting and evaluating their research data. Solutions to research problems encountered are also discussed. Seminar is required beginning in the second semester and continues throughout each student's program.

**02399 Doctoral Dissertation. 9 credits.**

This course is required for the completion of the PhD degree. The PhD candidate must submit a dissertation based on original research of a high scholarly standard that makes a significant contribution to knowledge in their chosen field.

**16267 Protein Chemistry: Applications. 1 credit.**

Protein Chemistry: Applications is a course suitable for all students interested in developing critical thinking skills through literature examples of protein activity and its regulation. Students and instructors will discuss literature that illustrates the in vitro reconstitutions, proteins structure/activity, and methods and logic of experimental design including critical control experiments. In addition, the discussions will include methods learned in the first-year curriculum that might have been applied but were not. From these analyses, students will hone their critical thinking and communication skills. Grading for this course will be based on 100 total points: 48 pts for classroom participation (metric attached) and 52 pts for a student-directed presentations/discussions (metric attached). At least three instructors will be involved in the grading of final presentations and the final score to be an average of each instructor's total score. The course will be capped at a maximum of 12 students; a minimum of 4 students will be required to offer this course. Instructors for this course will include current faculty members participating in the Biochemistry Graduate Program. The course will be offered every Spring semester. An overarching goal of the course is to prepare students for understanding the methods and logic underlying experimental design in modern biomedical research.

**16268 Protein Chemistry: Principles. 1 credit.**

Protein Chemistry: Principles is a course suitable for all students interested in developing critical thinking skills through literature examples of protein activity and its regulation. In this course, students and instructors will use the primary literature to learn and apply the practical formalisms in protein chemistry – including thermodynamics, kinetics, enzymology, and chemical biology – to the regulation of protein activity. Biology is governed by thermodynamic and kinetic principles, but these principles are often abstract to students. The purpose of this course is for students to develop utility in thermodynamic and kinetic principles and apply them to biological systems. The course will emphasize literature examples and expect students to learn these principles by working through problem sets provided by instructors. Students will be able to differentiate when thermodynamics or kinetics likely govern a given biological system and have a framework by which to analyze new systems. In addition, classroom discussions will include alternative methods and their relative merits. From these analyses, students will hone their critical thinking and communication skills. Grading for this course will be based on 225 total points: 90 pts for one in-class 90 min exam (90 pts, 10pts/lecture, 40% of grade), 90 pts for a student-directed presentations/discussions (metric attached, 40% of grade), and 45 pts on overall student participation in instructor-led discussion sessions (metric attached, 20% of grade). The course will be capped at a maximum of 12 students; a minimum of 4 students will be required to offer this course. Instructors for this course will include current faculty members participating in the Biochemistry Graduate Program. The course will be offered every Spring semester. An overarching goal of the course is to prepare students for understanding the methods and logic underlying experimental design in modern biomedical research.

**16274 Metabolism. 1 credit.**

This new elective course will be mainly a didactic based course that will comprehensively review subjective important to metabolism. the topics covered will range from carbohydrate metabolism to oxidative phosphorylation to lipid and amino acid metabolism. There will be a strong focus of these topics in health and disease, especially as they related to the cardiovascular system, cancer, diabetes, and immune system function. The depth of coverage within each topic will not necessarily be comprehensive, but there may be a few aspects of each topic that will be highlighted by focusing on landmark studies or recent developments from published research articles. Although there will be a specifically assigned textbook, students will be encouraged to read relevant chapters from Fundamentals of Biochemistry (Voet). Professors will also have the option to provide a specific reading list from either the Fundamentals Textbook, original scientific papers and/or review articles required for reading.

**Required Courses as Needed****02002 Master's Thesis Continuation. 0 credits.**

This is a form of registration available to students who have completed all of the required coursework, including thesis credits but have not yet completed the writing of the Thesis. Continuation status is limited to three consecutive terms following the completion of Thesis credits.

**02003 Doctoral Dissertation Continuation. 0 credits.**

This is a form of registration available to students who have completed all of the required coursework, including dissertation credits but have not yet completed the writing of the Dissertation. Continuation status is limited to three consecutive terms following the completion of Dissertation credits.

**02299 Master's Thesis. 6-9 credits.**

Students in the Ph.D. degree program who cannot or elect not to complete that program may be allowed to transfer to the Master's program. This transfer must be approved by the student's advisor, the Program Director, the Chair, and the Graduate School. To transfer to the Master's Program, the student must be in good academic standing according to regulations established by the Graduate School.

Contact information: [gradschool@mcw.edu](mailto:gradschool@mcw.edu) | (414) 955-8218